Antimicrobial Stewardship: What, Why, and How

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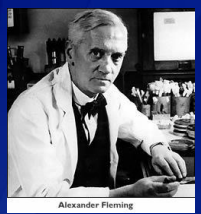
Objectives

- Understand the rationale and goals of antimicrobial stewardship
- Discuss primary drivers of timely and appropriate antimicrobial utilization
- Review strategies and success stories to improve antimicrobial use

Concern is Not New

1928



Alexander Fleming

Discovery of penicillin by Alexander Fleming

1945

- **…the microbes are educated to resist penicillin**
- **…a thoughtless person is morally responsible for the death of a man who finally succumbs to infection with a penicillin-resistant organism**

(Quote to NYTimes, June 26, 1945)

Antimicrobial Stewardship: A Rose by Any Other Name?

- *Antimicrobial stewardship* refers to strategic efforts to optimize antimicrobial prescribing
- The "name" has evolved over time
  - Antibiotic control
  - Antibiotic management
  - Antibiotic stewardship
  - Antibiotic safety

Overall Goal

Right drug
Right dose
Right duration

Recognize when not needed

Antibiotic Misuse

- Between 20-50% of antibiotic prescriptions are either unnecessary or inappropriate
  - *Given when they are not needed*
  - *The wrong antibiotic is chosen to treat an infection*
  - *Continued when they are no longer necessary*
  - *Given at the wrong dose*
  - *Broad spectrum agents are used to treat very susceptible bacteria*

Fishman N. Am J Med. 2006 Jun;119(6 Suppl 1):S53-61

The Challenge

- Antibiotics are commonly used "just in case"
  - *Broad coverage*
  - *Unclear criteria*
  - *Uncertain duration*
- General perception that there is (almost) no risk and (almost) all benefit to giving an antibiotic

Consequences of Inappropriate Use

- Antibiotics can harm patients
  - *C. difficile* infections
  - Adverse effects
- Resistance can lead to higher mortality and health care costs

Clostridium difficile Infections

Antibiotic exposure is the single most important risk factor

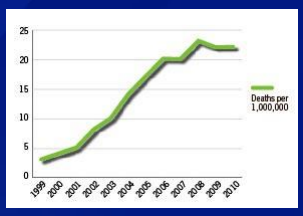
- Exposure to antibiotics increases the risk of *C. diff* infection by at least 3 fold for at least a month[1]
- Up to 85% of patients with *C. diff* infection have antibiotic exposure in the 28 days before infection[2]

1. Stevens et al. *Clin Infect Dis.* 2011 Jul 1;53(1):42-8
2. Chang HT et al. *Infect Control Hosp Epidemiol* 2007; 28:926i 931

Deaths due to *C. difficile* Infections

14,000 deaths in the US each year

- Deaths increased 400% between 2000 and 2007
- A stronger (hypervirulent) strain has emerged



Age-adjusted Rate of C. difficile as the Primary (Underlying) Cause of Death.
Source: CDC National Center for Health Statistics, 2012

Antibiotic-Related Adverse Events

- **Antibiotics account for nearly 1 in 5 (19.3%) drug-related adverse events**
  - >140,000 ER visits/year due to adverse effect of antibiotics
  - Admission required for 6.1% of adverse events
- **Side Effects: Fluoroquinolones (an example)**
  - Increased INR
  - QT interval prolongation
  - Tendon rupture
  - Risk of hypo- and hyperglycemia

Shehab et al. Clin Infecti Dis. 2008;47:735

Antibiotic Use Drives Resistance

For individuals

- **Getting an antibiotic increases a patient's chance of becoming colonized or infected with a resistant organism**
- **Risk of death higher for resistant infections**

Patel G et al. Infect Control Hosp Epidemiol 2008;29:1099-1106
Zaoutis TE et al. Pediatrics 2005;114:942-3
Talon D et al. Clin Microbiol Infect 2000;6:376-84

Effect of Antibiotic Use in Individuals

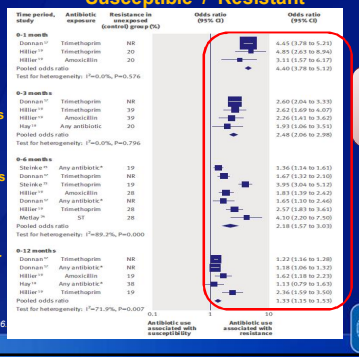
Susceptible / Resistant

At 1 month

Up to 3 months

Up to 6 months

Up to 1 year



Increased resistance right of line

Costelloe C et al. BMJ. 2010;340:c2096

Higher Mortality due to Resistance

- Methicillin resistant vs. susceptible *S. aureus (MRSA vs/ MSSA)*
  - *Mortality is nearly double*[1,2]
- Carbapenam resistant *Klebsiella pneumoniae* (CRKP vs/ CSKP)
  - *Mortality is 4-5 times higher*[3]

1. Clin. Infect. Dis.36(1).53i 59 (2003);
2. Infect. Control Hosp Epi.28(3).273i 279 (2007);
3. Infect Control Hosp Epi 2008;29:1099-1106

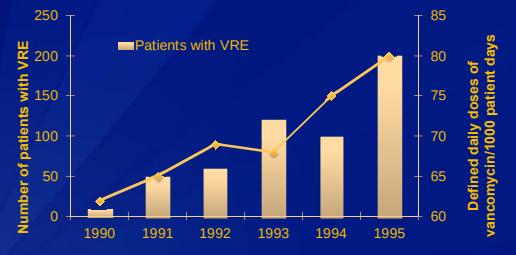
Antibiotic Use Drives Resistance

Within healthcare settings

- Increasing use of antibiotics increases the prevalence of resistant bacteria in hospitals

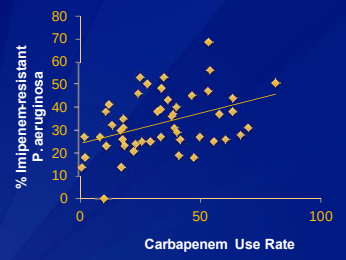
Patel G et al. *Infect Control Hosp Epidemiol* 2008;29:1099-1106
Zaoutis TE et al. *Pediatrics* 2005;114:942-9
Talon D et al. *Clin Microbiol Infect* 2000;6:376-84

Vancomycin-resistant *enterococci* (VRE) Increased with Vancomycin Use



Kim et al. JID 1999:179:163

Imipenem-resistant *P. aeruginosa* Increased with carbapenem use rate



- 45 long-term acute care hospitals (LTACH)

r = .0.41, p = .004
(Pearson correlation coefficient)

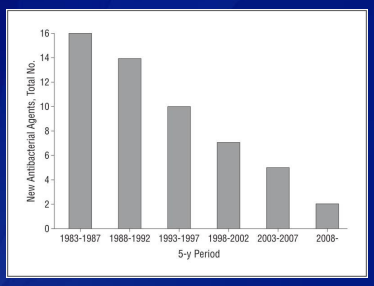
2002-03 (59 LTACH years)

Gould et al. ICHE 2006;27:923-5

Antimicrobial Resistance

- "Imminent crisis in the control of infectious diseases"
  - IOM report, 2003 *Microbial Threats to Health: Emergence, Detection, and Response*
- "…One of the world's most pressing public health problems"
  - *Joint Statement on Antibiotic Resistance from 25 National Health Organizations and the CDC, 2012*
- Antibiotic resistance is among CDC's top concerns

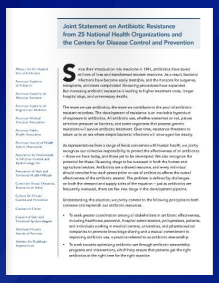
Reason for Concern:
Declining New Antimicrobials in the U.S.



- Drug development takes 10 years
- ~$400-800 million per approved agent
- No new gram (-) coverage in the pipeline

Spellberg. Arch Intern Med. 2011; 171(12): 1080–1081.

Joint Statement on Antibiotic Resistance
from 25 National Health Organization and the CDC


Joint Statement on Antibiotic Resistance from 25 National Health Organizations and the Centers for Disease Control and Prevention

- "The development of resistance is an inevitable byproduct of exposure to antibiotics."
- "…the way we use antibiotics today impacts how effective they will be in the future in other patients."
- "We jointly recognize our collective responsibility to protect to effectiveness of all antibiotic."

http://www.cddep.org/publications/

The Public Health Perspective

- **Antibiotics are a Shared Resource**
  - Antibiotic use in one patient can impact the effectiveness in another
  - If everyone does not use antibiotics wisely, we will all suffer the consequences
  - Antibiotics are becoming a scarce resource

Rationale for Antimicrobial Stewardship

- Improve Patient Care and Safety
  - Prevent C. Diff
  - Minimize Adverse Events
- Reduce Resistance
  - Decrease deaths
  - Preserve antimicrobial effectiveness

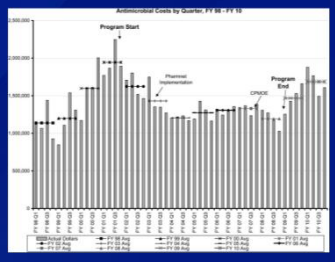
Additional Benefit: Cost Savings

- Improving antibiotics use saves money
  - Comprehensive programs have consistently demonstrated a decrease in antimicrobial use with annual savings of $200,000 - $900,000
- Cost savings due to:
  - Less pharmacy expenditure
  - Limiting increased costs associated with resistant infections (Length of stay, Readmission)

IDSA/SHEA Guidelines for Antimicrobial Stewardship Programs
http://www.journals.uchicago.edu/doi/pdf/10.1086/510393

Cost Savings from Stewardship

- **Antimicrobial utilization costs fell 45.9% during program**
  - $44,181 per 1000 patient days (PD) to $23,933
- **Increased 32.3% within 2 years when was program ended**
  - $31,653 / 1000 PD
  - Equiv. to $2 million



Standiford et al. ICHE. 2012;33:338-345

Antimicrobial Stewardship

How?

Antimicrobial Stewardship

Approaches to improving antimicrobial use

- Antimicrobial Stewardship "Program"
- Test and Refine Specific "Interventions"

Antimicrobial Stewardship Program

- Focus: Hospital-based
- Who (Team):
  - ID physician
  - ID-trained pharmacist
  - Administrative support
- Two Core strategies:
  - Prospective audit with intervention and feedback
  - Formulary restriction and preauthorization

GUIDELINE

Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America Guidelines for Developing an Institutional Program to Enhance Antimicrobial Stewardship

Infectious Diseases Society of America / Society of Healthcare Epidemiology of America Guidelines

Dellit at al. CID 2007:44

Prospective Audit

- An ID physician or pharmacist reviews orders and intervenes with modification of order and feedback to prescriber
- Results in improved use, decreased costs
- Caveats:
  - Time and labor intensive
  - Many settings do not have capacity
  - Providers may not be receptive

Formulary restriction and preauthorization

- Specific antibiotics cannot be ordered without authorization
- Useful in response to healthcare-associated outbreak

Impact of Fluoroquinolone Restriction on Rates of *C. difficile* Infection (CDI)

Kallen et al. Infect Control Hosp Epidemiol. 2009 Mar;30(3):264-72.

Formulary Restriction and Preauthorization

- Caveats:
  - Depends who is authorizing use
  - Impact on reducing resistance is not clear
  - Often results in increased use of other antibiotic alternatives

Limitations of the "Program" Approach

- Formally staffed stewardship programs are beyond the reach of most facilities
- Even a really good stewardship program cannot intervene on every patient getting antibiotics
- Programs create a perception that antibiotic stewardship is something that is done for you

Moving Stewardship to the Front Lines

- Every practitioner and each facility should embrace the responsibility to optimize antibiotic use
  - Not "create a stewardship program"
  - But "implement a specific intervention"
- Starting point: Identify specific ideas that people can do to improve antibiotic use

Antibiotic Driver Diagram

- CDC partnered with experts in stewardship and with the Institute for Healthcare Improvement (IHI)

Broke the process of prescribing and administering antibiotics into discrete steps	Drivers
Determined what specific actions could improve each of those steps	Change Ideas

- Result: A "Driver Diagram and Change Package" for antibiotic use in hospitals

http://www.cdc.gov/getsmart/healthcare/learn-from-others/driver-diagram/introduction.html

What are the 'Drivers' of Appropriate Use?

- **Appropriate initiation**
  - What to treat. What not to treat.
  - Obtaining cultures
  - Choosing based on guidelines and local susceptibility
- **Appropriate administration and de-escalation**
  - Correct dosing, route, and timing
  - Stop or change based on culture
  - Reconciling antibiotics at all transition in care

'Drivers' of Appropriate Use (Continued)

- Leadership Support
- Culture of Quality Improvement
- Stewardship Infrastructure/Champions
- Data monitoring
- Availability of Expertise

Antimicrobial Stewardship

Success Stories

Antimicrobial Stewardship in a Community Hospital

- **Setting:** 535-bed community hospital in Michigan
- **Team:** 2 ID physicians, 3 critical care pharmacists
- **Intervention:**
  - **Prospective audit of 8 antimicrobials**
    - **3 carbepenams, 2 antifungals, daptomycin, linezolid, tigecycline**
  - **Pharmacist evaluated each order (M-F)**
  - **Feedback given to providers**
    - **Approve, stop, de-escalate**
    - **Obtain an ID consult**

Malani et al. Am J Infect Control. 2012; May 9

Antimicrobial Stewardship in a Community Hospital

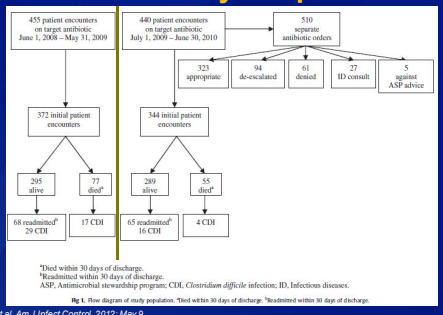


Fig 1. Flow diagram of study population. *Died within 30 days of discharge. †Readmitted within 30 days of discharge.

Malani et al. Am J Infect Control. 2012; May 9

Antimicrobial Stewardship in a Community Hospital

- **Clinical Outcomes**
  - **An approximate 50% reduction in the odds of developing CDI**
  - **No increase in mortality at 30 days after discharge**
  - **No increase in readmission rate**
- **Economic Outcomes**
  - **Antimicrobial cost per patient-day decreased from $10.16 to $8.81**
  - **Antimicrobial budget decreased by 15.2% (Total savings of $228,911)**
  - **There was a 25.4% decrease in use of the target antimicrobials**

Malani et al. Am J Infect Control. 2012; May 9

Antimicrobial Stewardship in a Rural Hospital

- **Setting:** 141-bed community hospital in rural Northwest
- **Team:** Pharmacist-led (non-ID), Remotely located ID physician
- **Intervention:**
  - Targeted review of six antimicrobials
    - Pip/Tazo, imipenam, cilastatin, ertapenam, vancomycin, linezolid, daptomycin
  - Weekly teleconference ñroundingòwith ID physician
  - Streamlined Therapy
    - Eliminated unnecessary combinations
    - Recommended more narrow spectrum
  - Dose optimization

Yam et al. Am J of Healht-System Pharm. 2012 ;(69):1142-8

Antimicrobial Stewardship in a Rural Hospital

Outcomes

- Number of interventions increased from 2 to 7 per week
- Streamlining was most common intervention
  - 44% before program, 96% after program began
- C. diff infections decreased from 5.5 to 1.6 (cases/10,000 pt days)
- Antimicrobial purchase costs decreased
  - $13,521 per 1,000 pt days (baseline) to
  - $ 9,756 (2010) to
  - $ 6,583 (2011 Quarter 1-2)

Yam et al. Am J of Health-System Pharm. 2012 ;(69):1142-8

An Antibiotic 'Time Out'

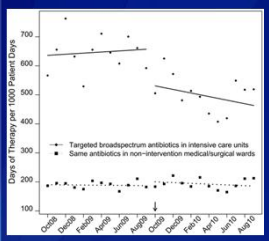
- The 'time out' concept is borrowed from surgery
- A concrete point in time dedicated to reviewing antimicrobial choice and duration
  - Reappraise therapy when more clinical data are available (usually in 48-72 hours)
  - Decide about continuation, narrowing therapy and specify a duration
- Recommended changes are better received and more likely to be followed at a later time point

ICU Antibiotic 'Time Out'

- **Setting:** 3 ICUs in tertiary-care medical center
- **Person:** Pharmacist
- **Intervention:**
  - Record review of all ICU patient on antibiotics at days 3 & 10 of therapy
    - 3rd gen cephalosporin, carbepenems, pip/taz, fluoroquinolone
  - Recommendation for optimization given by progress note and verbal feedback
  - Acceptance of recommendation by ICU attending

Walker et al. ICHE .2012;33(4):354

ICU Antibiotic 'Time Out' Results



- Broad spectrum use decreased
  - 644 to 503 days of therapy/1,000 pt days
  - Cost savings of $95,000/year
- *C. diff* infections
  - ICU: Decreased 11 to 6 cases
  - Control wards: Increased 87 to 116 cases
- Meropenem susceptibility increased from 78.2% to 83.4% in ICU isolates

Walker et al. ICHE .2012;33(4):354

Low Hanging Fruit

Transition from IV-to-oral

- VA Hospital reviewed their use of fluoroquinolone by route of administration
  - Of all IV fluoroquinolone prescriptions, 90.9% could have been converted to oral route
  - Avoidable IV fluoroquinolone use accounted for 46.8% of all fluoroquinolone use

Jones M, *et al.* ICHE 2012; 33(4):362-7

Low Hanging Fruit

Eliminate double anaerobic coverage

- Double coverage: metronidazole given with another agent that covers anaerobes
  - Excluding courses given for C. diff, cholangitis, and cholecystitis treatment
  - Reviewed metronidazole use from 2006-2010 at 128 acute-care VA facilities
  - Of 781,708 days of therapy, nearly 1 in 4 orders (23.5%) fulfilled criteria for possible redundancy

Huttner B, et al. JAC 2012; 67(6):1537-9.

Measurement

- Antibiotic Use Module
  - National Healthcare Safety Network (NHSN) module
  - Provides facilities a mechanism to report and analyze antimicrobial use
  - Antimicrobial use is captured by pharmacy information software
    - Launched, but in early stages of uptake
    - Dependent on pharmacy IT vendors to provide service

http://www.cdc.gov/nhsn/PDFs/pscManual/11pscAUBcurrent.pdf
http://www.sidp.org/Resources/Documents/SIDP_Stewardship_Vendor_List_9_5_12.pdf

Antimicrobial Stewardship

Conclusions

Antimicrobial Prescribing is Complex

- Knowledge in microbiology, infectious diseases, and pharmacology is required
- Information for decisions is available at different time points (and may change)
- Many different people and departments are involved

Prescribing: An Act within a System

An individual may prescribe appropriately but what about...

- New clinical information
- Care transitions and hand-offs

Successful approaches to achieve appropriate use reach beyond the prescriber

Take-Home Points

- Appropriate antimicrobial use is important for healthcare quality and safety
- Many opportunities exist to improve antimicrobial prescribing
  - *Education is not enough*
  - *Stewardship doesn't need to be a program*
  - *Small interventions can have big impact*

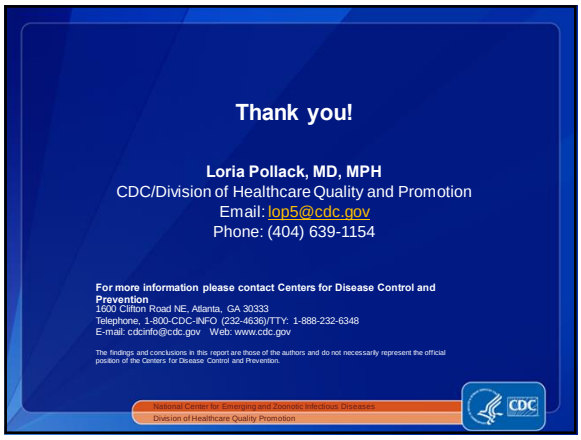
Antimicrobial Stewardship

Where to find resources?

Resources on *Get Smart for Healthcare* Website – *For your use!*

- Fact sheets and fast facts
- Slide sets
- Tools to start a program
- Press kit to raise awareness

http://www.cdc.gov/getsmartforhealthcare/


Thank you!
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The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.
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Division of Healthcare Quality Promotion
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